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NGUYEN, QUANG	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,484	CONTRERAS ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *73-90,92-95,97-107 and 109-112* is/are pending in the application.

4a) Of the above claim(s) *74-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *90,92-95,97-107 and 109-112* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/8/09;11/11/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 2/25/2010 was entered.

Claims 73-90, 92-95, 97-107, 109-112 are pending in the present application.

Claims 74-89 were withdrawn previously from further consideration because they are directed to an invention nonelected with traverse in the reply filed on 8/9/06.

Accordingly amended claims 90, 92-95, 97-107 and 109-112 are examined on the merits herein.

Response to Amendment

The rejection under 35 U.S.C. 112, first paragraph, for lack of Written Description was withdrawn upon further consideration.

The rejection under 35 U.S.C. 103(a) as being unpatentable over Martinet et al. (Biotechnology Letters 20:1171-1177, 1998; IDS) in view of JP 8336387 (12/24/96; IDS), Nakanishi-Shindo et al. (J. Biol. Chem. 268:26338-26346, 1993; IDS) and Chiba et al. (J. Biol. Chem. 41:26298-26304, 1998; IDS) was withdrawn in light of Applicant's amendment, particularly with respect to the new limitation "wherein the Och1 dsruption is the sole genetic disruption of the Golgi mannosyl transferases acting in N-glycosylation of said strain".

With respect to the presently amended claims, it is noted that in the prior art Nakanishi-Shindo et al (J. Biol. Chem. 268:26338-26346, 1993;IDS) showed that a double mutant of *och1 mnn1* was required to obtain Man8 as a predominant glycoform in *S. cerevisiae*, whereas a och1 single mutant produced a mixture of Man8, Man9, and

Man10 N-glycan **with Man9 being the dominant form**; Chiba et al (J. Biol. Chem. 41:26298-26304, 1998; IDS) reported obtaining Man5GlcNAc2 in *S. cerevisiae* using a **och1 mnn1 mnn4 triple mutant and an α-1,2-mannosidase**; the enzyme encoded by Mnn4 results in mannosylphosphorylation of the baker yeast's N-glycan, a modification which was known to be present in 30% of N-glycans in *Pichia* as shown by Grinna et al (Yeast 5:107-115, 1989). Accordingly, it would not have been obvious and/or those skilled in the art would not have reasonably expected that **a disruption of the Och1 gene alone** would have led to a production of Man8GlcNAc2 in an effective amount to permit the subsequent production of Man5GlcNAc2 as a predominant glycoform.

Claim Objections

Claims 90 and 107 are objected to because of the phrase "the Och1 disruption is the sole genetic disruption of Golgi mannosyl transferases acting in N-glycosylation of said strain". This is because prior to this limitation, the term "Och1" refers to both Och1 gene and Och1 protein. The examiner suggests the following phrase - - the Och1 gene disruption is the sole Golgi mannosyltransferase genetic disruption in said strain - - to overcome the above objection.

Enablement

Amended claims 90, 92-95, 97-107 and 109-112 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A genetically engineered strain of *Pichia*, wherein said strain is transformed with **a nucleotide sequence coding for a full-length *T. reesei* α-1,2-mannosidase**, wherein said *T. reesei* α-1,2-mannosidase is genetically engineered to contain an ER-retention signal and the genomic Och1 gene in said strain is disrupted such that said strain fails to produce a functional Och1 protein, and wherein as a result of expression of said *T. reesei* α-1,2-mannosidase said strain produces $Man_5GlcNAc_2$ as a predominant N-glycan structure or a predominant intermediate N-glycan structrure; a kit comprising the same strain and a method of reducing the glycosylation of an endogenous glycoprotein and/or a heterologous glycoprotein expressed in the same genetically engineered *Pichia* strain;

does not reasonably provide enablement for **a genetically engineered strain of *Pichia* transformed with other nucleotide sequences coding for a *T. reesei* α-1,2-mannosidase or functional part thereof to attain the specific desired result, a kit and a method of using the same strain as broadly claimed**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for the same reasons already set forth in the Office action mailed on 6/9/09 (pages 6-10). ***The same rejection is restated below.***

The present disclosure is not enabled for the instant broadly claimed invention for the reasons discussed below.

1. The breadth of the claims

The instant claims are directed to a genetically engineered strain of *Pichia* transformed with **a nucleotide sequence coding for a *T. reesei* α-1,2-mannosidase (including but not necessarily limited to a full length *T. reesei* α-1,2-mannosidase) or a functional part (fragment) thereof**, wherein the genomic OCH1 gene is said strain is disrupted and **as a result of the expression of said *T. reesei* α-1,2-mannosidase or said functional part, the genetically engineered strain produces $Man_5GlcNAc_2$ as a predominant N-glycan structure or a predominant intermediate N-glycan structure**; a kit comprising the same strain and a method of reducing glycosylation of an endogenous glycoprotein and/or a heterologous glycoprotein using the same strain.

2. The state and the unpredictability of the prior art

At about the effective filing date of the present application (6/30/2000), little was known about a modification of the protein glycosylation pathway in a *Pichia* yeast strain to generate Man5GlcNAc2 as a predominant N-glycan structure or a predominant intermediate N-glycan structure as evidenced at least by the teachings of Martinet et al (Biotechnology Letters 20:1171-1177, 1998; IDS) and Callewaert et al. (FEBS Letters 503:173-178, 2001). In contrast, there are several known double and triple mutants of *Saccharomyces cerevisiae* that have been characterized to produce $Man_5GlcNAc_2$ and/or $Man_8GlcNAc_2$ as a predominant glycoform species (Nakanishi-Shindo et al, J. Biol. Chem. 268:26338-26346, 1993; IDS; and Chiba et al, J. Biol. Chem. 41:26298-26304, 1998; IDS). Additionally, *T. reesei* α-1,2-mannosidase was overexpressed in a *pichia pastoris* strain, however the expression and/or activity of *T. reesei* α-1,2-

mannosidase was not sufficient to generate $Man_5GlcNAc_2$ as the predominant glycoform species (see Martinet et al and Callewaert et al references cited above). Several years after the effective filing date of the present application, Choi et al (PNAS 100:5022-5027, 2003) disclose that **a proper length of the α-1,2-mannosidase catalytic domain is one of several factors that determine the yield of $Man_5GlcNAc_2$ in *P. pastoris* Och1 mutant strains** (see at least page 5026, col. 1, second full paragraph). Moreover, as is well recognized in the art any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. There is a high degree of unpredictability associated with the use of the claimed embodiment as evidenced by the teachings of Rudinger in discussing peptide hormones. Rudinger stated that "The significance of particular amino acids and sequences for different aspects of biological activity (for this instance the enzymatic activities of α-1,2-mannosidase or glucosidase II) can not be predicted a priori but must be determined from case to case by painstaking experimental study (Page 6, first sentence of Conclusions *In* J.A. Parsons, ed. "Peptide hormones", University Park Press, 1976; IDS). Furthermore, it should be further emphasized that the relationship between the sequence of a peptide and its tertiary structure associated for its activity is not well understood and is not predictable (Ngo et al., *In* Merz et al., ed. "The protein folding problem and tertiary structure prediction", Birkhauser, 1994; IDS). Since the prior art at the effective filing date of the present application does not provide any guidance regarding to the aforementioned issues, it is

incumbent upon the instant specification to do so. Furthermore, the physiological art is also recognized as unpredictable (MPEP 2164.03).

3. The amount of direction or guidance provided

Apart from disclosing the use of an expression vector encoding the full-length *T. reesei* α-1,2-mannosidase for transforming a *Pichia pastroris* strain whose genomic OCH1 gene is disrupted to attain a predominant N-glycan structure or a predominant intermediate N-glycan structure (see at least examples 2-3 and Figures 6-7 and 10), the instant specification fails to provide sufficient guidance (exemplification is part of a guidance) for a skilled artisan on how to make and use any encoded fragment or functional part of a *T. reesei* α-1,2-mannosidase for producing Man5GlcNAc2 as a predominant N-glycan structure or a predominant intermediate N-glycan structure. In addition to a high degree of unpredictability associated with the make and/or use of an enzyme fragment having a specific desired property as discussed above, it should be noted that full-length *T. reesei* α-1,2-mannosidase has a pH optimum of 5.0 while most enzymes active in the ER and Golgi apparatus of yeasts have pH optima that are between 6,5 and 7.5 (Gerngross, US 2002/0137134, IDS; see at least paragraph 68), it is unclear whether any fragment of the *T. reesei* α-1,2-mannosidase would still be stable and still sufficient active in the less than optimal environment of a yeast's ER to yield Man5GlcNAc2 as a predominant N-glycan structure or a predominant intermediate N-glycan structure. As already noted above, several years after the effective filing date of the present application, Choi et al (PNAS 100:5022-5027, 2003) disclose that **a proper length of the α-1,2-mannosidase catalytic domain is one of several factors**

that determine the yield of $Man_5GlcNAc_2$ in *P. pastoris* Och1 mutant strains (see at least page 5026, col. 1, second full paragraph).

As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> That scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the are; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues set forth above, the breadth of the claims, and the state and the unpredictability of the relevant art, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

Response to Arguments

Applicants' arguments related to the above rejection in the Amendment filed on 10/9/09 (pages 13-14) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Applicants argue basically that the art may have collectively demonstrated the difficulties in producing $Man_5GlcNAc_2$ but there is no indication in the cited art that the difficulties were a result of employing fragments of *T. reesei* α-1,2-mannosidase of varying lengths. Applicants also argue that those skilled in the art would readily ascertain enzymatically active fragments of *T. reesei* α-1,2-mannosidase, such as its

catalytic domain, and would reasonably expect that such enzymatically active fragments of *T. reesei* α-1,2-mannosidase would be able to produce $Man_5GlcNAc_2$ as a predominant N-glycan structure or a predominant intermediate N-glycan structure in a strain as claimed. With respect to the cited Choi reference, there was no actual data showing the differences in length of the "catalytic domains" employed or the differences in the yield of $Man_5GlcNAc_2$; and that *T. reesei* α-1,2-mannosidase was not among the enzymes being investigated in these experiments. The Rudinger reference is merely making a generalized statement regarding modification to a "critical structural region of a protein" such as a conservative substitution and that enzymatically active fragments of *T. reesei* α-1,2-mannosidase do not include modifications to a "critical structural region of a protein" such as a "conservative substitution" in the catalytic domain. Accordingly, it would not require undue burden for a skilled artisan to make and use the presently claimed invention.

First, there was no evidence of record in either the prior art or in the instant specification that any enzymatically active fragment of *T. reesei* α-1,2-mannosidase has been successfully targeted to the ER and sufficiently stable and active to produce $Man_5GlcNAc_2$ as a predominant N-glycan structure or a predominant intermediate N-glycan structure in any genetically engineered methylotrophic yeast, let alone in genetically engineered Pichia strain as claimed. As already noted in the above rejection, the instant specification fails to provide sufficient guidance (exemplification is part of a guidance) for a skilled artisan on how to make and use any encoded fragment or functional part of a *T. reesei* α-1,2-mannosidase for producing Man5GlcNAc2 as a

predominant N-glycan structure or a predominant intermediate N-glycan structure. In addition to a high degree of unpredictability associated with the make and/or use of an enzymatically active fragment having a specific desired property, **it should be noted that full-length *T. reesei* α-1,2-mannosidase has a pH optimum of 5.0 while most enzymes active in the ER and Golgi apparatus of yeasts have pH optima that are between 6,5 and 7.5 (Gerngross, US 2002/0137134, IDS; see at least paragraph 68), it is unclear whether any enzymatically active fragment of the *T. reesei* α-1,2-mannosidase would still be stable and still sufficient active in the less than optimal environment of a yeast's ER to yield Man5GlcNAc2 as a predominant N-glycan structure or a predominant intermediate N-glycan structure**. Additionally, Choi et al (PNAS 100:5022-5027, 2003) also disclosed that **a proper length of the α-1,2-mannosidase catalytic domain is one of several factors that determine the yield of $Man_5GlcNAc_2$ in *P. pastoris* Och1 mutant strains** (see at least page 5026, col. 1, second full paragraph).

Second, with respect to Applicant's arguments on the Choi reference Choi et al stated explicitly "Although these constructs and several others resulted in glycans, which were 70-80% or more (Man)5-GlcNAc)2 (Fig. 3C and D), **>56% of the fusions resulted in <10% (Man)5-(GlcNAc)2 (Table 1). These data clearly emphasize the importance of choosing the proper combination of (i) a localization sequence and (ii) an α-1,2-mannosidase of the proper length. Fungal α-1,2-mannosidase with acid pH optima (e.g., *P. cintrinium and A. nidulans*), when expressed as fusions with the leader library, generally resulted in low (Man)5-(GlcNAc)2 yields (data not**

shown) consistent with previous findings (11, 21)" (page 5026; col. 1, second last paragraph). Therefore, with enzymatically active fragment of fungal *T. reesei* α-1,2-mannosidase of which length and in combination with which specific ER-retention signal that would yield $Man_5GlcNAc_2$ as a predominant N-glycan structure or a predominant intermediate N-glycan structure in a genetically engineered strain of Pichia as broadly claimed? Once again, it should be noted that ***T. reesei* α-1,2-mannosidase has a pH optimum of 5.0 (acidic pH)**. Although Choi et al did not use specifically *T. reesei* α-1,2-mannosidase in the disclosed experiments, they studied α-1,2-mannosidase derived from many sources, including fungal α-1,2-mannosidase with acidic pH optima, all of which involve in the same enzymatic reaction for processing N-glycan structures as *T. reesei* α-1,2-mannosidase.

Third, with respect to Applicants' arguments on the Rudinger reference please note that the citation of the Rudinger reference is to show simply that it is recognized in the prior art at the effective filing date of the present application that the significance of particular amino acids and sequences for different aspects of biological activity (for this instance the generation of Man5GlcNAc2 as a predominant N-glycan structure or a predominant intermediate N-glycan structure in a genetically engineered Pichia strain) can not be predicted a priori but must be determined from case to case by painstaking experimental study. Moreover, please also note that the instant claims encompass the use of any encoded enzymatically active fragment of *T. reesei* α-1,2-mannosidase of any length, including the deletion of any conservative fragment(s) outside of the catalytic domain. Furthermore, it should be further emphasized that **the relationship**

between the sequence of a peptide and its tertiary structure associated for its activity is not well understood and is not predictable (Ngo et al., *In* Merz et al., ed. "The protein folding problem and tertiary structure prediction", Birkhauser, 1994; IDS).

Since the prior art at the effective filing date of the present application does not provide any guidance regarding to the aforementioned issues, it is incumbent upon the instant specification to do so. Accordingly, due to the lack of sufficient guidance provided by the specification regarding to the issues set forth above, the breadth of the claims, and the state and the unpredictability of the relevant art, it would have required undue experimentation for one skilled in the art to make and use the instant broadly claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Amended claims 90, 92-95 and 105 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2, 4-6, 9 and

14 of U.S. Patent No. 7,252,933 for the same reasons already set forth in the Office action mailed on 6/9/09 (page 22). ***The same rejection is restated below.***

Although the conflicting claims are not identical, they are not patentably distinct from each other because a methylotrophic yeast strain transformed with a nucleotide sequence coding for the *T.reseei* α-1,2-mannosidase encoded by SEQ ID NO: 14 and a kit comprising the same in issued U.S. Patent No. 7,252,933 encompasses the *Pichia pastoris* strain (claim 2), a methylotrophic yeast strain in which the OCH1 gene has been disrupted (claim 6), the *T.reseei* α-1,2-mannosidase is engineered to contain the peptide HDEL (claims 4-5) and the expression of *T.reseei* α-1,2-mannosidase is directed by a promoter of a gene selected from the group consisting of AOXI, an AOXII, GAP, YPT1 and FLD, would also fall within the scope of claims 90, 92-95 and 105 of the present application.

Amended claims 90, 92-95 and 105 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 7,507,573 for the same reasons already set forth in the Office action mailed on 6/9/09 (pages 22-23). ***The same rejection is restated below.***

Although the conflicting claims are not identical, they are not patentably distinct from each other because a genetically engineered *Pichia* strain, wherein said strain is engineered to express (1) a *Trischoderma reesei* α-1,2-mannosidase or a functional part thereof, (2) an N-acetylglucosaminyltransferase I (GnTI) or a functional part thereof, and (3) a beta-1,4-galactosyltransferase (GalT) or a functional part thereof, and the

genomic OCH1 gene of said strain is disrupted in the issued U.S. Patent No. 7,507,573 anticipates the claimed genus of a genetically engineered strain of *Pichia* and a kit comprising the same in the application being examined and, therefore, a patent to the genus would, necessarily, extend the rights of the species or sub- should the genus issue as a patent after the species of sub-genus.

Amended claims 90, 92-95, 97-107 and 109-112 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 5-8, 13-14 and 17-28 of U.S. Patent No. 6,803,225 for the same reasons already set forth in the Office action mailed on 6/9/09 (pages 23-24). ***The same rejection is restated below.***

The claims of the present application differ from the claims of the issued US Patent 6,803,225 in reciting specifically a genetically engineered *Pichia* yeast strain expressing *T. reesei* α-1,2-mannosidase, and a recited Markush group of specific promoters used to express *T. reesei* α-1,2-mannosidase and/or glucosidase II.

The claims of the present application can not be considered to be patentably distinct over claims 5-8, 13-14 and 17-28 of U.S. Patent No. 6,803,225 when there is a specific disclosed embodiment of the issued US patent that teaches the use of vectors coding for *T. reesei* α-1,2-mannosidase and its expression under the control of at least AOX1 promoter (see all the examples). Accordingly, the claims of the issued US patent fall within the scope of claims 90, 92-95, 97-107 and 109-112 of the present application.

This is because it would have been obvious to an ordinary skilled artisan to modify the claims of the issued US patent by also using vectors coding for *T. reesei* α-1,2-mannosidase and its expression under the control of at least AOX1 promoter for making and using the genetically engineered *Pichia* yeast strain, that support the instant claims. An ordinary skilled artisan would have been motivated to do this because this embodiment is explicitly disclosed or taught in the issued US patent as a preferred embodiment.

In the amendment filed on 10/9/09 (page 14), Applicants indicated that a terminal disclaimer would be filed once the claims are found allowable.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN/
Primary Examiner, Art Unit 1633